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EDITORIAL COMMENT

TMVR: Continuing the Paradigm Shift in Valvular Heart Disease Therapy

Hype or Hope?*

Howard A. Cohen, MD, Brian P. O'Neill, MD

Transcatheter treatment of valvular disease has been performed for more than 3 decades (1). Transcatheter mitral valvuloplasty has achieved widespread acceptance for patients with symptomatic mitral stenosis and favorable anatomy (2). Most recently, transcatheter aortic valve replacement (TAVR) has advanced rapidly and has become an accepted treatment for patients who are inoperable or at high risk for surgical aortic valve replacement (3). The procedure is now being evaluated in patients with intermediate risk for surgery ("valve creep"). In the mitral valve (MV) arena, MV percutaneous repair for severe mitral regurgitation (MR) with the MitraClip (Abbott Vascular, Santa Clara, California) is now approved for patients with MR due to "degenerative" MR who are at high surgical risk and is being rigorously evaluated as well in the United States (COAPT [Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients With Functional Mitral Regurgitation] trial, NCT01626079) in patients at high surgical risk with severe "functional" MR and left ventricular (LV) dysfunction (4). The device has the CE Mark and has been used extensively in Europe in both functional and degenerative MR. Multiple technologies that mimic surgical MV repair are now being actively evaluated and are in the early stages of development, but have not been rigorously evaluated in randomized trials. As of this writing, the pulmonic, tricuspid, aortic, and mitral valves have all been replaced by percutaneous techniques (3,5–8).

Transcatheter mitral valve replacement (TMVR) has not progressed as rapidly as TAVR for several reasons. First, MV repair (rather than replacement) has been accepted as preferable whenever possible in degenerative MR (9). Second, the MV is significantly more complex, both anatomically and physiologically, than the aortic valve. Whereas there is no true aortic valve annulus, the MV annulus is a complex anatomic structure that has been extensively studied and imaged and that plays a significant physiological role, along with the leaflets, chordae, and papillary muscles, in maintaining the integrity and function of the MV, as well as of the left ventricle (10). Off-label use of percutaneous aortic valves has been successfully utilized in the MV position to treat degenerated bioprosthetic valves, as well as failed mitral ring repairs (7,8). This strategy is facilitated by the rigid annulus of the bioprosthetic valve or surgical ring, which presents a platform for the valve-in-valve. In addition, there are several reports of TMVR using balloon-expandable valves in patients with severe calcific mitral disease who were thought to be inoperable by standard techniques (11,12). As with TAVR, the calcific disease may be important in these patients, providing a rigid platform to anchor the prosthetic valve. The native noncalcified MV has no such rigid ring to anchor a percutaneous valve, although patented technology has now been developed that may provide such a platform or anchor for a percutaneous device. Any percutaneous MV replacement technology will need to incorporate a similar type of platform or technology to achieve secure positioning of the valve.

Cheung et al. (13) recently reported the first-in-man series of transapical MV replacement using the Tiara device (Neovasc, Richmond, British Columbia), with

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From the Temple University Heart and Vascular Institute, Philadelphia, Pennsylvania. Dr. Cohen is the Medical Director of and has stock options in CardiacAssist, Inc.; and is a principal investigator for Abbott Vascular. Dr. O'Neill is a consultant to CardiacAssist, Inc.; and his father is a stockholder in Neovasc. William O'Neill, MD, served as Guest Editor for this paper.

excellent results in 2 patients with severe MR and depressed LV function. In this issue of the *Journal*, the authors report their initial experience with the FORTIS valve (Edwards Lifesciences, Irvine, California) in 3 patients with severe functional MR

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(14). Their report is the first to provide a longer-term follow-up indicating not only the feasibility of the procedure, but also the efficacy and safety at 6 months. Patients were evaluated by a heart team and were declined for surgery due to their comorbidities. The valve was delivered successfully in all patients via a transapical approach. There was less than minor residual leak in all patients, and all were discharged after the successful procedure. At follow-up, transmitral and left ventricular outflow tract (LVOT) gradients in all patients were acceptable, and all showed improvement in New York Heart Association functional classification at 3 and 6 months.

The authors are to be congratulated for their contribution to the field of TMVR in this group of high-risk patients. Their report highlights several important aspects of the procedure that will apply to all future valve designs. Computed tomography will continue to play a vital pre-planning role in accurate sizing of the MV annulus to strike a delicate balance between undersizing (and paravalvular leak) and oversizing (and LVOT obstruction) (15). New imaging software packages will allow for computed tomography coregistration and improved online echocardiographic guidance as well. Given the complex interaction between the aortic and mitral valves, 3-dimensional printing may also serve an important role in modeling the heart and allowing insertion of differently sized "model valves" before the actual procedure, as demonstrated in caval valve implant for severe tricuspid regurgitation (16). Transesophageal echocardiography will continue to be critical to the success of the procedure by confirming accurate transapical access to maintain coaxiality of the valve system and assessing, in real time, residual MR and gradients across the MV and LVOT (9,13).

As the field matures, several challenges will need to be addressed. Current technology requires insertion of large delivery sheaths via the LV apex. As many nonsurgical candidates already have severe LV dysfunction, transseptal delivery systems have the potential to decrease the morbidity and improve the safety of these procedures. Furthermore, these devices will undoubtedly become smaller and more user friendly, thus facilitating their delivery. In those patients in whom transapical delivery is preferable, novel closure device systems are currently in development for percutaneous closure. Finally, we must remember that this report is truly of a short-term follow-up and that we have much to learn regarding the safety of this approach in terms of the durability of the bioprosthesis, the alignment and continued security of the device, the potential for erosion, the possibility of outflow tract obstruction, and the need for anticoagulation over the long term (9). Recently, the U.S. trial of the FORTIS valve was halted due to cases of valve thrombosis, emphasizing the need for continued research regarding anticoagulation and biocompatibility.

This is an exciting time in the evolutionary and revolutionary treatment of valvular heart disease, with an opportunity to improve the lives of our patients. As noted by many investigators, patients are frequently being denied treatment because they are thought to be "too sick" (9). If nothing else, what we have learned from the TAVR experience is that we can treat these very sick patients, improve the quality of their lives, and do this in a cost-effective fashion. We should not lose sight of the fact that MV surgery (replacement and repair) by experienced operators is a very mature "art form" that provides effective treatment for our patients (17) and that will set a very high bar for any percutaneous therapy that is developed. It is reasonable at the outset, therefore, to consider TMVR in those patients who need MV replacement, but who are thought by the multidisciplinary team to be at high risk for surgery.

REPRINT REQUESTS AND CORRESPONDENCE: Dr. Howard A. Cohen, Temple University Heart and Vascular Institute, Suite 945, Parkinson Pavilion, 3401 North Broad Street, Philadelphia, Pennsylvania 19104. E-mail: howard.cohen@tuhs.temple.edu.

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